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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,343	08/26/2005	Wang Min	21108.0021U2	5753

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,343	MIN ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/7/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *11-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/US03/22847.

Claims 1-64 are pending. Claims 11-64 are withdrawn. Claims 1-10 are under consideration.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-10) in the reply filed on December 7, 2007 is acknowledged. The traversal is on the ground(s) that Bishopric et al. (form PTO-1449) is not prior art under 35 USC 102(a) because the disclosure of mutant thioredoxins in Bishopric et al. is the inventor's own work. This is not found persuasive because for the purpose of determining lack of unity, prior art is considered as "everything made available to the public anywhere in the world by means of written disclosure (including drawings and other illustrations)..provided that such making available occurred prior to the relevant date" (see MPEP 1850, 1843.01 and 1878.01(a)). In the instant case, the relevant date is the filing date of the priority application (60/401,073 - August 2, 2002). Since the reference of Bishopric et al. was published on June 28, 2002, Bishopric et al. is indeed prior art. Therefore, the technical feature linking the inventions of Groups I-XII does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Thus, unity of invention is lacking.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 7, 2007.

Claim for Domestic Priority

Applicants' claim for domestic priority under 35 USC 119(e) to US provisional application 60/401073, filed 8/02/02, is acknowledged.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on September 9, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner. Initialed form PTO-1449, PTO/SB/08A and/or PTO/SB/08B are attached.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 1-10, as written, do not sufficiently distinguish over thioredoxins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products, such as being “isolated”. Even though the claims are drawn to mutant thioredoxins, such mutants can exist naturally. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of “isolated” as taught by the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4, 6, and 9 and claims 5-6 and 10 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "the amino acid alteration" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitation "the substitution or deletion" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 6 recites the limitation "the substitution or deletion" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 9 recites the limitation "the amino acid alteration" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 4-6 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-6 and 10 recite the phrases “residue 32 or an analogous residue”, “residue 35 or an analogous residue”, or “residue 69 or an analogous residue”. The metes and bounds of the phrases in the context of the above claims are not clear to the Examiner. Since applicants do not provide the reference amino acid sequence for the wild-type thioredoxins, it is not clear which amino acid in a thioredoxins polypeptide is “residue 32 or an analogous residue”, “residue 35 or an analogous residue”, or “residue 69 or an analogous residue”. Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrases. Examiner requests clarification of the above phrases. For examination purposes, Examiner has broadly interpreted the phrases to encompass substitution or deletion of any amino acids having sulfhydryl groups (cysteine residues).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to **(A)** a mutant thioredoxin, **(B)** a mutant thioredoxin comprising an amino acid alteration that decreases the number of sulfhydryl groups, **(C)** a mutant thioredoxin comprising a cysteine substitution or deletion, or **(D)** a mutant thioredoxin comprising substitution or deletion at residues 32, 35, 69 or an analogous residue, wherein said mutant thioredoxin of **(A)-(D)** is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." The examiner has interpreted the claims broadly to encompass any or all polypeptides having thioredoxin activity and having resistance to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide, wherein said polypeptide comprises **(A)** any modification, **(B)** any amino acid alteration that decreases the number of sulfhydryl groups, **(C)** any cysteine substitution or deletion, or **(D)** substitution or deletion at residues 32, 35, 69 or an analogous residue deletion, and additionally any other amino acid modifications at any amino acid positions. Therefore, the claims are drawn to a genus of polypeptides having the function recited in claims 1 and/or 7 but having unknown structure.

In *University of Calfornia v. Eli Lilly & Co.,* 43 USPQZd 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, (or) chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The recitation of "thioredoxin" fails to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in UC California v. Eli Lilly, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the

genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of "thioredoxin" proteins, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

The claims are drawn to polypeptides having unknown structure, encompassing any or all variants, recombinant and mutants of any or all thioredoxin isolated from any source having thioredoxin activity and the properties recited in claims 1 and/or 7, wherein said polypeptides **A)** any modification, **(B)** any amino acid alteration that decreases the number of sulfhydryl groups, **(C)** any cysteine substitution or deletion, or **(D)** substitution or deletion at residues 32, 35, 69 or an analogous residue deletion, and additionally any other amino acid modifications at any amino acid positions. The specification only describes a mutant of only one thioredoxin, the thioredoxin having the amino acid sequence of SEQ ID NO:1, wherein said mutant consists of an amino acid substitution at position 32, 35 and/or 69 of SEQ ID NO:1 and wherein said mutant continues to have thioredoxin activity and is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide. While MPEP

2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In view of the widely variant species encompassed by the genus, this one example of a single species of a thioredoxin (SEQ ID NO:1) is not enough and does not constitute a representative number of species to describe the whole genus of any or all variants, recombinant and mutants of any or all thioredoxin isolated from any source or SEQ ID NO:1 comprising **A)** any modification, **(B)** any amino acid alteration that decreases the number of sulfyhydryl groups, **(C)** any cysteine substitution or deletion, or **(D)** substitution or deletion at residues 32, 35, 69 or an analogous residue deletion, and any other amino acid modifications at any amino acid positions, and there is no evidence on the record of the relationship between the structure of the thioredoxin of SEQ ID NO:1 and the structure of any or all variants, recombinant and mutants of any or all thioredoxin isolated from any source or SEQ ID NO:1. Therefore, the specification fails to describe a representative species of the genus comprising polynucleotides having any structure.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant of the thioredoxin having the amino acid sequence of SEQ ID NO:1, wherein the mutant consists of an amino acid substitution at position 32, 35 and/or 69 of SEQ ID NO:1 and wherein said mutant continues to have thioredoxin activity and is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide, does not reasonably provide enablement for mutant thioredoxins having unknown structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to **(A)** a mutant thioredoxin, **(B)** a mutant thioredoxin comprising an amino acid alteration that decreases the number of sulfyhydryl groups, **(C)** a mutant thioredoxin comprising a cysteine substitution or deletion, or **(D)** a mutant thioredoxin comprising substitution or deletion at residues 32, 35, 69 or an analogous residue, wherein said mutant thioredoxin of **(A)-(D)** is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide.

The breadth of the claims.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." The examiner has interpreted the claims broadly to encompass any or all polypeptides having thioredoxin activity and having resistance to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide, wherein said polypeptide comprises **(A)** any modification, **(B)** any amino acid alteration that decreases the number of sulfyhydryl groups, **(C)** any cysteine substitution or deletion, or **(D)** substitution or deletion at residues 32, 35, 69 or an analogous residue deletion, and additionally any other amino acid modifications at any amino acid positions. Therefore, the claims are drawn to polypeptides having the function recited in claims 1 and/or 7 but having unknown structure.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides of virtually any structure. In the instant case, the specification only enables a mutant of the thioredoxin having the amino acid sequence of SEQ ID NO:1, wherein said mutant consists of an

amino acid substitution at position 32, 35 and/or 69 of SEQ ID NO:1, wherein said mutant continues to have thioredoxin activity and is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide.

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification.

While enzyme isolation techniques, recombinant and mutagenesis techniques were known in the art at the time of the invention, e.g. mutagenesis, and it is routine in the art to screen for variants comprising multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

In the absence of: (a) rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function, (b) a correlation between structure and function of thioredoxin, the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. One of skill in the art would have to test these infinite possible polypeptides to determine (1) which mutants have thioredoxin activity or the properties recited in claims 1 and/or 7, (2) the specific substrates targeted by such proteins and (3) how to use those polypeptides not having thioredoxin activity. While enablement is not

precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance which respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims

The state of prior art, the relative skill of those in the art, and predictability or unpredictability of the art.

Since the amino acid sequence of the mutant determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, neither the specification or the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any polypeptides having the same biological function as that of the polypeptide of SEQ ID NO:1 or the properties recited in claims 1 and/or 7 or predict the function of a polypeptide from its primary structure. In addition, the art does not provide any teaching or guidance as to (1) which amino acids within the polypeptides of SEQ ID NO:1 (other than the amino acid at position 32, 35 and 69 of SEQ ID NO:1) can be modified and which ones are conserved such that one of skill in the art can make the recited

polypeptides having the same biological activity as that of the polypeptide of SEQ ID NO:1 and the properties recited in claims 1 and/or 7, (2) which segments of the polypeptide of SEQ ID NO:1 are essential for activity, and (3) the general tolerance of thioredoxin to structural modifications and the extent of such tolerance. The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions.

The amount of direction or guidance presented and the existence of working examples.

The specification only enables a mutant of the thioredoxin having the amino acid sequence of SEQ ID NO:1, wherein said mutant consists of an amino acid substitution at position 32, 35 and/or 69 of SEQ ID NO:1, wherein said mutant continues to have thioredoxin activity and is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide. However, the speciation fails

to provide any information as to (1) specific substrates associated with thioredoxins, (2) structural elements required in a polypeptide or SEQ ID NO:1 having thioredoxin activity, (3) which are the structural elements in a polypeptide or SEQ ID NO:1 that are essential to display thioredoxin activity or (4) structural elements in any polypeptide that are essential for having the properties recited in claims 1 and/or 7 (other than residues 32, 35 or 69). No correlation between structure and function of having thioredoxin activity has been presented. There is no information or guidance as to which amino acid residues in the polypeptides of SEQ ID NO: 1 or any thioredoxins can be modified and which ones are to be conserved to create a polypeptide displaying thioredoxin activity or the properties recited in claims 1 and/or 7.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability of the prior art in regard to structural changes and their effect on function and the lack of knowledge about a correlation between structure and function, an undue experimentation would be necessary one having ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics recited in the claims are unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Warren et al.

Claims 1-10 are drawn to a mutant thioredoxin comprising a cysteine substitution or deletion or a substitution or deletion at residues 32, 35, 69 or an analogous residue, wherein said mutant thioredoxin is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." Since applicants do not provide the reference amino acid sequence for the wild-type thioredoxins, it is not clear which amino acid in a thioredoxins polypeptide is “residue 32 or an analogous residue”, “residue 35 or an analogous residue”, or “residue 69 or an analogous residue”. Therefore, Examiner has broadly interpreted the phrases to encompass substitution or deletion of any amino acids having sulfhydryl groups (cysteine residues).

Bishopric et al. (form PTO-1449) discloses a thioredoxin comprising a substitution at a cysteine residue at position 32 and 35, or an analogous residue of 69.

Examiner takes the position that the mutant thioredoxins of Bishopric et al. inherently possesses the same material structure and functional characteristics as the enzyme of the instant invention since (1) both enzymes have the same amino acid substitutions (2) both enzymes function as thioredoxins with decreased oxidizing effects, and (3) the Office does not have facilities for examining and comparing applicant's enzyme with the enzyme of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the mutant thioredoxins of the prior art does not possess the same material structure and functional characteristics of the claimed thioredoxin). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Figzgerald* et al., 205 USPQ 594. Therefore, the reference of Bishopric et al. anticipates claims 1-10.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Yodoi et al.

Claims 1-10 are drawn to a mutant thioredoxin comprising a cysteine substitution or deletion or a substitution or deletion at residues 32, 35 and/or 69 or an analogous residue, wherein said mutant thioredoxin is resistant to oxidizing effects of cytokines or reactive oxygen species or S-nitrosylation of a SH-group by nitrous oxide.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." Since applicants do not provide the reference amino acid sequence for the wild-type thioredoxins, it is not clear which amino acid in a thioredoxins polypeptide is "residue 32 or an analogous residue",

"residue 35 or an analogous residue", or "residue 69 or an analogous residue". Therefore, Examiner has broadly interpreted the phrases to encompass substitution or deletion of any amino acids having sulfhydryl groups (cysteine residues).

Yodoi et al. (EP 0 853 088 A2 – form PTO-892) discloses a thioredoxin comprising a substitution at a cysteine residue at position 32, 35, 62, 69 and/or 73 which are stable in oxidizing conditions (column 1, lines 3-5, Figure 1 on page 8 and Column 4 line 30 through column 5, line 14). Examiner takes the position that the mutant thioredoxins of Yodoi et al. inherently possesses the same material structure and functional characteristics as the enzyme of the instant invention since (1) both enzymes have the same amino acid substitutions (2) both enzymes are stable in oxidizing conditions, and (3) the Office does not have facilities for examining and comparing applicant's enzyme with the enzyme of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the mutant thioredoxins of the prior art does not possess the same material structure and functional characteristics of the claimed thioredoxin). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Figzgerald* et al., 205 USPQ 594. Therefore, the reference of Yodoi et al. anticipates claims 1-10.

Examiner Comment

Other Relevant Art

Liu et al. (reference A26 – form PTO-1449) discloses a thioredoxin comprising a substitution at a cysteine residue at position 32 and 35 (abstract), but is not available as prior art because the reference is not by another.

Conclusion

Claims 1-10 are rejected.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652